Synopsis

Introduction

Cancer deaths are the world's second-leading cause after cardiovascular disorders. In cancer treatment, the primary challenge is drug resistance due to mutations. Therefore, the search for targets effective against cancer with resistance is crucial. The literature reveals that Benzfused heterocyclic compounds, such as harmine, harminol, and staurosporine, have been effective as Dyrk1a/mTOR inhibitors in nature. Dyrk1a is a target for cancer treatment.

The Pyridopyridazine core, a Benzfused nitrogen-containing heterocyclic compound, was explored in the first series. Seven pyridopyridazine analogues were prepared and evaluated in vitro against 60 cell lines, demonstrating effectiveness with a 40 percent inhibition rate. Another Benzfused ring explored in this study is quinoline, as it has shown huge potential as a prominent anticancer scaffold, exemplified by several FDA-approved drugs such as camptothecin, topotecan, and irinotecan, as well as currently approved drugs like olutasidenib, Mitapilvat, and FX-909.

Methodology

Two series of Benzfused compounds were designed and synthesized as series-I and Series-II. Series-I is based on the pyridopyridazine scaffold, and series-II is based on 2-chloroquinoline moiety. A total 40 compounds were synthesized from both series-I & II. Compounds were characterized by FT-IR, NMR, and Mass spectral data. The 28 compounds were screened for *in-vitro* anticancer activity against a 60-cell lines. The compounds of series-I were also evaluated for anti-microbial activity using cup-plate method against E. coli and S. aureus strains In Series-II In the initial step, the quinoline aldehyde core is synthesized by Vilsmeier-Haack reaction and then azine derivatives. The *in-vitro* anticancer screening was conducted using 60 cell lines